

## LISTING OF CLAIMS

This listing of claims will replace all prior versions, and listings of claims in the application:

1. **(Currently amended)** A method of selectively inhibiting an immune response to one or more selected autoantigenic protein antigens of multiple sclerosis comprising:
- exposing purified or isolated antigen presenting cells (APCs), which present an autoantigenic protein antigen of multiple sclerosis against which selective inhibition of an immune response is desired, to an immunosuppressive composition comprising one or more factors secreted by a glioblastoma cell, wherein the one or more factors secreted by the glioblastoma cells have the following characteristics:
- ~~(a) induce APCs to induce T cells to undergo apoptosis; and wherein the one or more factors (a) have a minimum molecular mass of about 40 kDa,~~
  - ~~(b) bind to an anion exchange column, (c) do not bind to a cation exchange column, (d) maintain the ability to induce APCs in the pH range of about 2-11 or following heat exposure up to about 56°C, (e) substantially lose the ability to induce APCs following heat exposure above about 56°C or following trypsin exposure, and (f) are not immunoprecipitated from glioblastoma culture supernatant by neutralizing antibodies against TGF- $\beta$ 1, TGF- $\beta$ 2, TGF- $\beta$ 3, IL-6, calcitonin gene related peptide (CGRP), or M-CSF~~
  - (b) molecular weight greater than about 40 kDa;
  - (c) ability to bind to anion, but not cation, exchange columns;
  - (d) maintain an ability to induce APCs to induce T cells to undergo apoptosis
    - (i) within the pH range of 2 to 11, (ii) following heat exposure up to about 56° C, and (iii) following immunoprecipitation of TGF- $\beta$ 1, TGF- $\beta$ 2, TGF- $\beta$ 3, IL-6, calcitonin gene related peptide (CGRP), and M-CSF from the composition; and
  - (e) lose the ability to induce APCs to induce T cells to undergo apoptosis
    - (i) following heat exposure above 56° C, or (ii) after exposure to trypsin;
- and

introducing a therapeutically effective amount of the APCs exposed to the immunosuppressive composition into a subject in whom a selectively inhibited immune response to the antigen is desired, wherein introduction of the APCs inhibits the immune response of the subject to the antigen.

2. **(Currently amended)** A method of selectively inhibiting an immune response to one or more selected autoantigenic protein antigens of multiple sclerosis, comprising:

exposing purified or isolated antigen presenting cells (APCs), comprising macrophages, monocytes, dendritic cells, and/or B cells, to an immunosuppressive composition comprising one or more factors secreted by one or more glioblastoma cells,

wherein the APCs present an autoantigenic protein antigen of multiple sclerosis

against which selective inhibition of an immune response is desired;

and wherein incubation of the APCs with the one or more factors results in effects comprising:

- (a) \_\_\_decreasing expression of MHC class II antigens and CD 80/86 on the surface of the monocytes and the dendritic cells,
- (b) \_\_\_increasing expression of IL-10 in the monocytes and dendritic cells, and
- (c) \_\_\_decreasing the expression of IL-12 in the monocytes and dendritic cells, ~~and (d) inducing the APCs to induce T cells to undergo apoptosis;~~

and wherein the one or more factors secreted by the glioblastoma cells have the following characteristics:

- ~~(1) have a minimum molecular mass of about 40 kDa, (2) bind to an anion exchange column, (3) do not bind to a cation exchange column,~~
- ~~(4) maintain the ability to induce APCs in the pH range of about 2-11 or following heat exposure up to about 56°C, (5) substantially lose the ability to induce APCs following heat exposure above about 56°C or following trypsin exposure, and (6) are not immunoprecipitated from glioblastoma culture supernatant by neutralizing antibodies against TGF- $\beta$ 1, TGF- $\beta$ 2, TGF- $\beta$ 3, IL-6, calcitonin gene related peptide (CGRP), or M-CSF; and~~
- (1) induce APCs to induce T cells to undergo apoptosis;

- (2) molecular weight greater than about 40 kDa;
- (3) ability to bind to anion, but not cation, exchange columns;
- (4) maintain an ability to induce APCs to induce T cells to undergo apoptosis (i) within the pH range of 2 to 11, (ii) following heat exposure up to about 56° C, and (iii) following immunoprecipitation of TGF- $\beta$ 1, TGF- $\beta$ 2, TGF- $\beta$ 3, IL-6, calcitonin gene related peptide (CGRP), and M-CSF from the composition; and
- (5) lose the ability to induce APCs to induce T cells to undergo apoptosis (i) following heat exposure above 56° C, or (ii) after exposure to trypsin; and

introducing a therapeutically effective amount of the APCs exposed to the immunosuppressive composition into a subject in whom a selectively inhibited immune response to the antigen is desired, wherein introduction of the APCs inhibits the immune response of the subject to the antigen.

**3-9. (Cancelled)**

**10. (Currently amended)** The method of claim 9~~1~~, wherein the ~~purified or isolated~~ APCs are obtained from a subject suffering from an autoimmune disease, and the ~~isolated or purified~~ APCs are repetitively exposed to one or more peptide fragments of the autoantigenic protein of the autoimmune disease.

**11. (Cancelled).**

**12. (Currently amended)** The method of claim ~~10~~1, wherein the autoantigenic protein is selected from the group consisting of comprises myelin basic protein (MBP), type II collagen, acetyl choline receptor (AChR), nuclear proteins, and pancreatic islet cell antigens.

**13. (Currently amended)** The method of claim ~~2~~1, wherein the APCs are selected from the group consisting of monocytes, macrophages, and dendritic cells.

14. **(Currently amended)** The method of claim 13, wherein the APCs ~~comprise~~  
consist of monocytes.

15. **(Cancelled).**

16. **(Currently amended)** The method of claim 910, wherein the APCs comprise  
monocytes isolated or purified from the subject's blood.

17. **(Previously presented)** The method of claim 2, wherein the glioblastoma cell is  
selected from the group consisting of SNB 19 (DSMZ no. 325), A172 (ATCC no. CRL-1620),  
U87 MG (ATCC no. HTB-14), U138 MG (ATCC no. HTB-16) and U373 MG (ECACC  
no. 89081403).

18-24. **(Cancelled).**

25. **(Original)** The method of claim 2, wherein introducing the APCs into the  
subject comprises administering the APCs by a route selected from the group consisting of  
intravenous, subcutaneous, intramuscular, and intraperitoneal administration.

26-27. **(Cancelled).**

28. **(Currently amended)** A method of selectively inhibiting an immune response to  
one or more selected autoantigenic protein antigens of multiple sclerosis comprising:

exposing purified or isolated antigen presenting cells (APCs), which present an  
autoantigenic protein antigen of multiple sclerosis against which selective inhibition of an  
immune response is desired, to an immunosuppressive composition comprising one or more  
factors secreted by a glioblastoma cell, wherein the one or more factors secreted by the  
glioblastoma cell have the following characteristics:

- (a) induce APCs to induce T cells to undergo apoptosis,~~and wherein the one~~  
~~or more factors (a) have a minimum molecular mass of about 40 kDa;~~
- ~~(b) bind to an anion exchange column, (c) do not bind to a cation~~  
~~exchange column, (d) maintain the ability to induce APCs in the pH range~~

~~of about 2-11 and following heat exposure up to about 56°C, (e) substantially lose the ability to induce APCs following heat exposure above about 56°C and following trypsin exposure, and (f) are not immunoprecipitated from glioblastoma culture supernatant by neutralizing antibodies against TGF-β1, TGF-β2, TGF-β3, IL-6, calcitonin gene related peptide (CGRP), or M-CSF~~

- (b) molecular weight greater than about 40 kDa;
- (c) ability to bind to anion, but not cation, exchange columns;
- (d) maintain an ability to induce APCs to induce T cells to undergo apoptosis
  - (i) within the pH range of 2 to 11, (ii) following heat exposure up to about 56° C, and (iii) following immunoprecipitation of TGF-β1, TGF-β2, TGF-β3, IL-6, calcitonin gene related peptide (CGRP), and M-CSF from the composition; and
- (e) lose the ability to induce APCs to induce T cells to undergo apoptosis
  - (i) following heat exposure above 56° C, or (ii) after exposure to trypsin;and

introducing a therapeutically effective amount of the APCs exposed to the immunosuppressive composition into a subject in whom a selectively inhibited immune response to the antigen is desired, wherein introduction of the APCs inhibits the immune response of the subject to the antigen;

wherein the glioblastoma cell is selected from the group consisting of SNB 19 (DSMZ no. 325), A172 (ATCC no. CRL-1620), U87 MG (ATCC no. HTB-14), U138 MG (ATCC no. HTB-16), U373 MG (ECACC no. 89081403), T98G (ATCC no. CRL-1690), DBTRG-05MG (ATCC no. CRL-2020), M059K (ATCC no. CRL-2365), M059J (ATCC no. CRL-2366), and U118 MG (ATCC no. HTB-15).

29-33. **(Cancelled).**

34. **(Previously presented)** The method of claim 28, wherein incubation of monocytes, dendritic cells, and B cells with the one or more factors results in effects comprising:

(a) decreased expression of MHC class II antigens and CD 80/86 on the surface of the monocytes and the dendritic cells, without substantial effect on the expression of MHC class II antigens and CD 80/86 on the B cells;

(b) increased expression of IL-10 in monocytes and dendritic cells; and

(c) decreased the expression of IL-12 in monocytes and dendritic cells.

35-36. **(Cancelled).**

37. **(Previously presented)** The method of claim 2, wherein the glioblastoma cell is selected from the group consisting of T98G (ATCC no. CRL-1690), DBTRG-05MG (ATCC no. CRL-2020), M059K (ATCC no. CRL-2365), M059J (ATCC no. CRL-2366), and U118 MG (ATCC no. HTB-15).

38. **(New)** The method of claim 2, wherein the autoantigenic protein comprises myelin basic protein (MBP).

39. **(New)** The method of claim 28, wherein the autoantigenic protein comprises myelin basic protein (MBP).